Premium

MicroRNA, gene regulation: What 2024 Nobel Prize for Medicine was awarded for

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Written by Kaunain Sheriff M

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The Nobel Prize for Medicine this year has been awarded to scientists Victor Ambros and Gary Ruvkun for their discovery of microRNA — tiny molecules which play a crucial role in how genes function.

“Gene regulation by microRNA, first revealed by Ambros and Ruvkun, has been at work for hundreds of millions of years. This mechanism has enabled the evolution of increasingly complex organisms,” the Nobel press release for the announcement stated.

Why did Ambros and Ruvkun study microRNA?

According to the press release, the scientists were honoured for their “discovery of a fundamental principle governing how gene activity is regulated”. Here is an illustration to explain just what this means.

Think of chromosomes, which carry genetic information in the form of DNA, as a large toolbox. Every cell in the body has the same toolbox, containing identical tools (or genes). But different cells need to use different tools depending on their job — while a nerve cell might grab a tool that helps send signals, a muscle cell might choose a different tool to enable movement.

The key to these differences is gene regulation, a process that helps each cell pick the right tools for its specific tasks. In other words, only the appropriate set of genes is activated in each type of cell. Ambros and Ruvkun were curious about how gene regulation works. Their research led them to the discovery of microRNA, which provided a whole new way of understanding how bodies of complex organisms such as humans function.

Why is understanding gene regulation significant?

Genetic information is stored in DNA inside the nucleus of each cell. This information is copied to the mRNA, a molecule that contains the instructions that direct cells to synthesise appropriate proteins. Proteins handle all kinds of

important jobs in the body, such as making muscles contract or helping nerves communicate.

Different tissues in the body create different proteins, depending on their specific functions. This differentiation among cells is governed by gene regulation, which effectively turns on or off specific genes in a cell in order to allow it to carry its specific task.

Faults in gene regulation can result in serious diseases like cancer, diabetes, or autoimmune conditions. Understanding gene regulation, thus, holds the key to understanding — and potentially treating — many of these conditions.

In the 1960s, scientists found that specialised proteins, called transcription factors, could bind to specific regions of DNA, and control which genetic messages were produced. These transcription factors essentially acted like switches, turning genes on or off depending on the needs of the cell. This was a huge leap in understanding how genes are regulated, and for many years, it seemed like the mystery of gene regulation had been mostly solved. Thousands of transcription factors were identified, and it appeared that the scientific community had figured out the key to how cells control the flow of genetic information.

Then, in 1993, this year's Nobel winners published findings that revealed an entirely new process by which genes are regulated, one which no one had anticipated.

How was microRNA discovered?

In the late 1980s, Ambros and Ruvkun were working under Nobel Prize-winning researcher Robert Horvitz, studying a tiny roundworm called C. elegans. Despite being just 1 millimetre long, this worm had many of the same cell types found in larger animals, making it an ideal candidate for understanding how tissues develop.

Ambros and Ruvkun were particularly interested in two genes in these worms: lin-4 and lin-14. These genes played important roles in determining when different cells matured. The scientists' curiosity was piqued when they noticed that certain

mutant worms had problems with this timing. Ambros discovered that lin-4 seemed to inhibit lin-14, but the scientific process behind this was unclear.

After setting up his lab at Harvard, Ambros began further investigating the lin-4 gene. To his surprise, he found that lin-4 produced a tiny RNA molecule that did not code for proteins like most genes do. Instead, this “micro” RNA simply blocked the activity of lin-14.

Meanwhile, Ruvkun, in his own lab, was closely examining the lin-14 gene when he discovered that lin-4 was not stopping the production of lin-14’s mRNA which carried genetic instructions for making its protein. Rather, it was preventing lin-14 from making the protein itself. As Ambros and Ruvkun compared their findings, a breakthrough emerged — the short RNA from lin-4 matched a specific part of lin-14’s mRNA, allowing it to latch on and effectively turn off lin-14’s protein production.

This discovery revealed a fascinating new way in which genes could be controlled through tiny RNA molecules now called microRNAs. Initially published in 1993, the discovery got little notice as most scientists believed that this peculiar process was limited to C. elegans.

However, everything changed in 2000 when Ruvkun’s team discovered another microRNA, called let-7, which was found across many species, including humans. This finding sparked widespread interest, leading to the identification of hundreds of microRNAs. Today, we know that microRNAs play a crucial role in gene regulation for nearly all multicellular organisms, including humans.